



Flagship Pioneering Unveils Omega Therapeutics and Appoints Seasoned BioPharma Executive Mahesh Karande as President and Chief Executive Officer

Omega Therapeutics is unleashing the human genome's native capacity to regulate genes and cure disease for a new era of genomic medicine

The Company's platform is focused on precise tuning of Insulated Genomic Domains (IGDs), the fundamental regulators, or GenomStats™, of the human genome, and has over 10 potential programs with unique targets to control disease

Proprietary Omega Controllers™ are a transformative therapeutics class that are designed to deliver precision genomic control

CAMBRIDGE, Mass., September 23, 2019 – [Flagship Pioneering](#), a unique life science innovation enterprise, today unveiled Omega Therapeutics™ – a genomics medicine company focused on selectively directing the human genome to treat and cure disease by precisely controlling genomic expression without changing nucleic acid sequences. Mahesh Karande has been appointed as the company's President, CEO and member of the Board of Directors. Mr. Karande was the former President and CEO of Macrolide Pharmaceuticals and a long-time Novartis AG executive where he held positions of increasing responsibility running large businesses in the U.S. and internationally. Flagship Pioneering developed and launched Omega Therapeutics through its innovation foundry, Flagship Labs.

Since its founding in 2017, under the leadership of David Berry, M.D., Ph.D., General Partner of Flagship Pioneering, Omega Therapeutics has created a proprietary platform that precisely tunes Insulated Genomic Domains (IGDs), the fundamental regulator, or GenomStats™, of the human genome, which are 3D closed-loop structures of DNA that control genomic activity, to unlock the native power of the genome to cure diseases. This enables the unique, rapid development of specific therapeutics that treat disease and help patients, without altering nucleic acid sequences, with implications across a variety of indications. Engineered genomic modulators, called Omega Controllers™, precisely tune genomic activity to desired therapeutic levels to address the biological root of disease. Our therapeutics are designed to be more specific and durable and, as such, potentially more effective therapeutic options for patients.

“By mapping the topology of the human genome and using computational biology, we have been able to identify the correct genomic target for a therapeutic influence. Omega's proprietary platform technology allows us to develop therapeutics for disease control, and potentially impact the way we treat and manage a broad range of illnesses,” said Dr. Berry. “In addition to our own capabilities for therapeutic development, our technology also presents the opportunity to partner and optimize other targeted in vivo and ex vivo therapeutics to enhance their ability to treat disease and further help a wide range of patient populations with significant unmet needs.”

Many health conditions, particularly complex diseases, are the result of malfunctions in the regulation of gene expression. Omega leverages the founding Flagship team's pioneering innovations that extended the breakthrough work on epigenetics by Richard Young, Ph.D., Professor of Biology, Massachusetts Institute of Technology, and Member of the Whitehead Institute, and Rudolf Jaenisch, M.D., Professor of Biology, Massachusetts Institute of Technology and Founding Member of the Whitehead Institute, who first described how genomic activity is controlled by 3D closed-loop structures of DNA, now called Insulated Genomic Domains (IGDs), that contain one or more genes and their regulatory elements.

These insulated, or closed-loop, structures ensure that interaction between the regulatory elements and gene(s) leading to gene expression is contained within the IGD. Diseases often manifest due to alterations in gene expression or changes in IGD structure. As such, the IGD is the fundamental regulator, or GenomStat, of the human genome. Omega is pioneering the discovery and development of precision Omega Controllers to control the GenomStat. By precisely tuning the GenomStat, Omega Controllers regulate single- or multi-gene expressions to desired levels to treat or cure disease. Scientific strategy and research and development will be led by Chief Science Officer, Thomas McCauley, Ph.D., former Shire executive and more recently CSO of Macrolide Pharmaceuticals and CSO of Translate Bio (formerly RaNA Therapeutics).

"Flagship is focused on discovering value and innovating well beyond the boundaries of current research in order to build first-of-their-kind companies. Omega's proprietary product-platform is taking an entirely new approach to tackling important, unsolved diseases," said Noubar Afeyan, Ph.D., Chief Executive Officer of Flagship Pioneering and Chair of Omega's Board of Directors. "The executive team, board of directors and scientific advisors have created an unparalleled company that fits the extraordinary scope of the therapeutic potential of Omega Controllers, a new class of medicines."

"The depth and breadth of our platform gives us the ability to create transformative genomic medicines that deliver specificity of targeting, tunability, and durability of single and multi-gene expression, all without altering nucleic acid sequences. Our platform enables us to develop proprietary Omega Controllers, a new class of therapeutics targeting the control of a wide range of diseases in unprecedented ways," said Mr. Karande. "With a team of world-class scientists, founders and advisors, we are already executing several ambitious early-stage discovery programs in the near-term, as we strengthen our platform to address the vast opportunity of treating diseases resulting from genomic malfunction or dysregulation."

Omega Therapeutics is targeting the biological root of disease and designing novel therapeutics and optimizing current therapies to potentially address a wide range of disease categories, including rare genetic diseases, immunology, inflammation, metabolic diseases and oncology.

The Omega Therapeutics Board of Directors:

- **David Berry, M.D., Ph.D.**, General Partner, Flagship Pioneering, Co-founder, Omega Therapeutics
- **Richard Young, Ph.D.**, Professor of Biology, Massachusetts Institute of Technology, Member, Whitehead Institute
- **Paul-Peter Tak, M.D., Ph.D.**, Chief Executive Officer, Kintai Therapeutics, Venture Partner, Flagship Pioneering, former Senior Vice President and Global Head of R&D for Immuno-inflammation, Oncology and Infectious Disease, as well as Chief Immunology Officer, GlaxoSmithKline (GSK)

- **Mary Szela**, Chief Executive Officer, TriSalus Life Sciences, former Chief Executive Officer, Novelion Therapeutics, and Chief Executive Officer, Melinta Therapeutics
- **Mahesh Karande**, President and Chief Executive Officer, Omega Therapeutics
- **Noubar Afeyan Ph.D.**, Co-founder and Chairman of the Board, Omega Therapeutics, CEO Flagship Pioneering

ABOUT MAHESH KARANDE, PRESIDENT AND CHIEF EXECUTIVE OFFICER

Mahesh Karande is deeply experienced in running biopharma businesses across discovery, preclinical development, clinical development, commercialization and product life-cycle management stages. He has strong leadership and operational experience combined with a global work history spanning the United States, Europe, Asia and Africa. Most recently, Mr. Karande, as President and CEO, took Macrolide Pharmaceuticals, from discovery into early development. Earlier, Mr. Karande spent several years at Novartis, leading various U.S. and international business units. Mr. Karande left Novartis to join Intarcia Therapeutics as VP and General Manager to lead the launch of their first product; a role he left to take the helm at Macrolide.

ABOUT OMEGA THERAPEUTICS™

Omega Therapeutics™ is a preclinical stage genomic medicine enterprise transforming medicine and patient care through precision genomic control. The company's platform is focused on selectively directing the human genome to treat and cure disease by precisely controlling genomic expression without changing nucleic acid sequences. We are developing precision therapeutics for a range of disease indications including rare genetic diseases, immunology, inflammation, metabolic diseases and oncology.

Founded by Flagship Pioneering, Omega has created a platform and knowledge base that identifies Insulated Genomic Domains (IGDs) and their biological functions in both healthy and diseased states across cell types. IGDs function as the fundamental regulators, or GenomStats™, of the human genome. This scientific insight drives our discovery and development of genomic modulators called Omega Controllers™, which we engineer to precisely tune genomic activity to desired therapeutic levels without altering the human genetic code. To learn more please visit our website: www.omegatherapeutics.com.

ABOUT FLAGSHIP PIONEERING

Flagship Pioneering conceives, creates, resources, and develops first-in-category life sciences companies to transform human health and sustainability. Since its launch in 2000, the firm has applied a unique hypothesis-driven innovation process to originate and foster more than 100 scientific ventures, resulting in over \$30 billion in aggregate value. To date, Flagship is backed by more than \$3.3 billion of aggregate capital commitments, of which over \$1.7 billion has been deployed toward the founding and growth of its pioneering companies alongside more than \$10 billion of follow-on investments from other institutions. The current Flagship ecosystem comprises 37 transformative companies, including: Axcella Health (NASDAQ: AXLA), Denali Therapeutics (NASDAQ: DNLI), Evelo Biosciences (NASDAQ: EVLO), Foghorn Therapeutics, Indigo Agriculture, Kaleido Biosciences (NASDAQ: KLDO), Moderna (NASDAQ: MRNA), Rubius Therapeutics (NASDAQ: RUBY), Seres Therapeutics (NASDAQ: MCRB), and Syros Pharmaceuticals (NASDAQ: SYRS). To learn more about Flagship Pioneering, please visit our website: www.FlagshipPioneering.com.

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